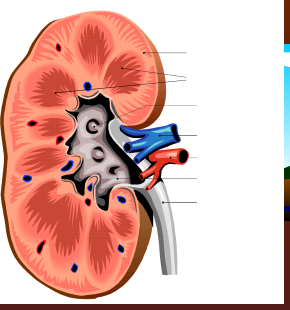

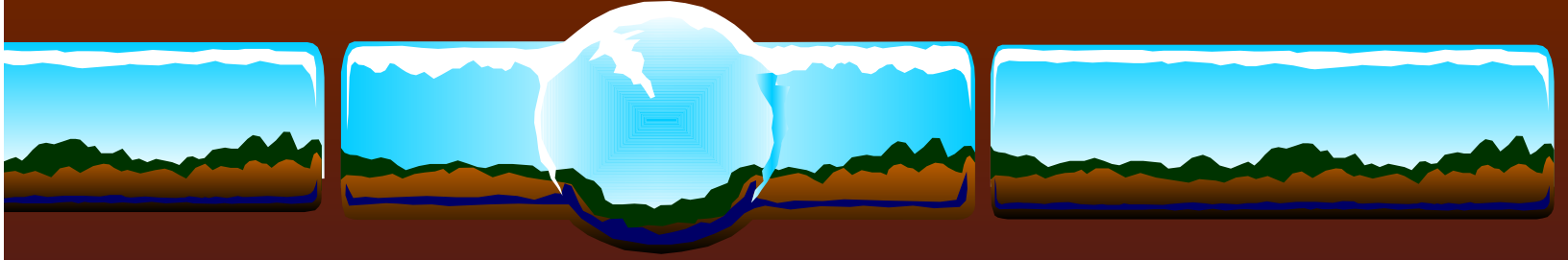

The Natural History of Atheromatous Renal Artery Stenosis (or, Is the Truth Out There?)

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17 Feb, 1999

Enabling Learning Objective

- Know the estimates of the incidence of renal artery stenosis as a contributor to ESRD, and the limitations of those estimates
- Know the literature regarding the progression of renal artery stenosis
- Know the survival rates for patients for renal vascular disease and their potential impact in selecting patients for intervention

Enabling Learning Objective

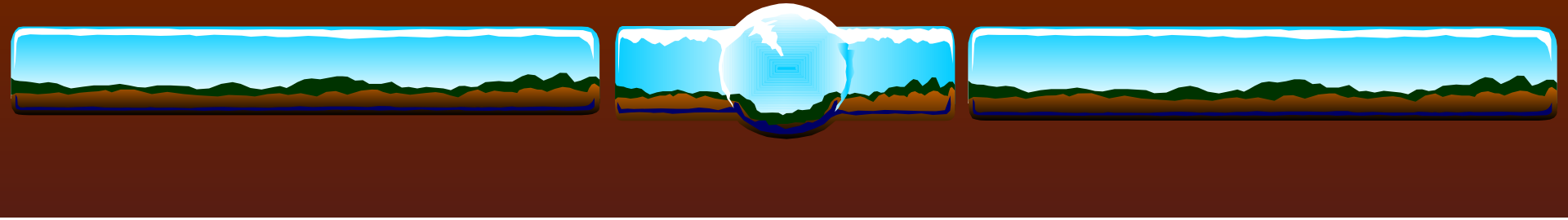
- Synthesize available evidence into preliminary local practice guidelines for this condition.

The Natural History of Atheromatous Renal Artery Stenosis--Outline

- Incidence
- Progression (especially from prospective trials)
- Survival

Incidence of atheromatous renal artery disease (ARD)

- Estimates are in large part based on autopsy studies and retrospective series (1, 2).
- Early interest focused only on blood pressure control. Progressive renal insufficiency was brought to wider attention by *Jacobsen* (3), although *Dean's* article (to follow) did follow serial renal function measurements.



Changing Profile of Incident ESRD Patients by Year of Incidence

Year of Incidence	Average Age	Percent Diabetic	Unadjusted Death Rate*	Adjusted** Death Rate*
1988	57.5	31.2	26	30
1989	58.3	32.8	26	28
1990	58.7	34.4	25	27
1991	59.2	36.1	26	27
1992	59.6	36.6	25	26
1993	60.0	36.4	25	25
1994	59.8	38.2	24	25
1995	59.6	40.6	23	24

* deaths per 100 patient years at risk in the first year of ESRD therapy

** adjusted for age, race, sex, and diabetes as the primary cause of ESRD

Source: Reference Tables A.1, A.14, E.14, and E.22

USRDS 1998

Incidence of atheromatous renal artery disease

- In a non-selected necropsy study, RAS >50% was found in 5% of patients under 64, compared to 18% between 65-74, and 42% over 75. There was severe bilateral stenosis in 50% of cases (1).

Incidence of atheromatous renal artery disease

- Another necropsy study with a mean age of 61 showed severe RAS in 17% of normotensive patients vs. 56% of hypertensive patients, with a 62% incidence in patients over 70 (1).
- Neither study evaluated renal function.

Incidence of atheromatous renal artery disease

- A prospective study with renal angiography (and perhaps the only one in this area) of all (64) patients starting renal replacement therapy in one unit (in England) over 18 months showed atherosclerotic renal artery stenosis in 10 patients (14%) *Scoble et al* (1).

Incidence of atheromatous renal artery disease

- All patients presenting with either difficult hypertension, asymmetrical kidneys, unexplained renal failure or systemic vascular disease underwent formal arteriography or digital subtraction angiography.

Incidence of atheromatous renal artery disease

- Of the 10, one declined surgery and was started on dialysis. Three had no procedures (surgical risk too high).
- Two had surgery (on splenorenal bypass and one hepatorenal bypass), with on with improved function, coming off dialysis (follow-up not mentioned), the other with no improved function. This patient also had a hemothorax as an operative complication.

Incidence of atheromatous renal artery disease

- Four patients had angioplasties (three bilateral).
- One patient had “significant improved function” (after renal artery clotting during procedure and bleeding from urokinase), one with stabilized function. Two had MI’s (one fatal) associated with angiography.
- Long-term follow-up not available.

Incidence of atheromatous renal artery disease

- Reviews continue to claim that ischemic renal disease is underdiagnosed as a cause of ESRD.
- The1998 USRDS reports lists “renal artery stenosis or occlusion” as a cause of ESRD in 1.8% of all patients from 1992-1996, 3.1% for those older than 64. This percentage is increasing every year, while the percent diagnosis for hypertension is decreasing.

Column Percents for Incidence of Treated ESRD by Detailed Primary Disease, Age, Sex, and Race for all Patients, 1992-1996[1]

			Age Group (% Age)			Sex (%)		Race (%)			
Primary Disease	Total 1992-96	% of Total[2]	<20	20 - 64	>64	Male	Female	White	Black	Asian	Nat Am
All ESRD (reference)	**332459**	**100.0**	**5155**	**171774**	**155530**	**176868**	**155591**	**212461**	**97753**	**10324**	**5044**
Diabetes	**130473**	**39.2**	**1.6**	**43.4**	**35.9**	**35.0**	**44.1**	**39.4**	**38.0**	**41.6**	**63.2**
. Type 1, juvenile type	46100	13.9	0.8	18.3	9.4	12.8	15.0	15.2	11.7	10.5	14.6
. Type 2, adult-onset or unspec. type	84373	25.4	0.8	25.1	26.5	22.1	29.1	24.2	26.3	31.1	48.7
Glomerulonephritis	**36499**	**11.0**	**31.7**	**13.1**	**7.9**	**12.5**	**9.2**	**11.7**	**9.0**	**17.8**	**9.0**
. Focal glomerulosclerosis, focal GN	6497	2.0	10.0	2.7	0.9	2.3	1.6	1.8	2.5	1.7	1.2
. Membranous nephropathy	1554	0.5	0.4	0.6	0.3	0.6	0.3	0.5	0.4	0.3	0.3
. Membranoproliferative GN, types 1&2	1284	0.4	2.5	0.5	0.2	0.4	0.3	0.4	0.2	0.7	0.4
. IgA nephropathy, Berger's disease	1080	0.3	1.3	0.5	0.1	0.4	0.2	0.4	0.1	1.3	0.4
. IgM nephropathy	121	0.0	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.2	0.0
. Rapidly progressive GN	1336	0.4	2.1	0.4	0.4	0.4	0.4	0.5	0.2	0.5	0.4
. Goodpasture's Syndrome	780	0.2	0.7	0.2	0.2	0.2	0.3	0.3	0.1	0.1	0.2
. Post infectious GN, SBE	214	0.1	0.1	0.1	0.0	0.1	0.1	0.1	0.0	0.0	0.1
. Glomerulonephritis (GN)	22749	6.8	13.2	7.8	5.5	7.8	5.8	7.3	5.4	12.5	5.7
. Other proliferative GN	884	0.3	1.3	0.3	0.2	0.3	0.2	0.3	0.2	0.5	0.2
Secondary GN/Vasculitis	**8122**	**2.4**	**9.1**	**3.4**	**1.2**	**1.5**	**3.5**	**2.4**	**2.5**	**2.7**	**2.0**
. Acute interstitial nephritis	346	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.0
Hypertensive/Large Vessel Disease	**93651**	**28.2**	**5.0**	**21.0**	**36.8**	**30.3**	**25.8**	**25.7**	**35.9**	**23.6**	**14.4**
. Hypertension (no primary renal dis.)	86403	26.0	4.6	20.3	33.0	27.8	23.9	22.5	35.5	22.7	13.6
Renal artery stenosis or occlusion	5894	1.8	0.4	0.6	3.1	2.0	1.5	2.6	0.4	0.7	0.7
. Cholesterol emboli, renal emboli	1354	0.4	0.0	0.1	0.7	0.5	0.3	0.6	0.1	0.2	0.2
Cystic/Hereditary/Congenital Dis.	**11648**	**3.5**	**24.4**	**4.5**	**1.7**	**3.7**	**3.3**	**4.5**	**1.6**	**2.6**	**1.9**

Incidence of atheromatous renal artery disease

- The most frequently cited study for the underdiagnosis of ARD is by *Mailloux et at* Cornell Medical College (1).
- This was a retrospective study of 683 patients who were initiated on dialysis were followed from 1970 to 1989 with follow-up through 1992.

Incidence of atheromatous renal artery disease

- A clinical diagnosis of renal vascular disease was defined as the clinical evidence of systemic atherosclerosis with either a positive renal angiogram or **suggestive radionuclide studies** in the absence of significant proteinuria and a benign urinary sediment, most often in a hypertensive setting.
- Patient demographics not given but presumably predominantly caucasian.

Incidence of atheromatous renal artery disease

- However, neither the 1994 study nor its antecedent in 1991 (1) specify how many patients had angiography or radionuclide studies, and of those how many had unilateral vs. bilateral disease.
- A call is in to Dr. Mailloux to clarify these issues.
- The limitations of radionuclide studies in patients with GFR's <30, and especially in ESRD, are well known, and will be elaborated on more in the Screening Section.

Incidence of atheromatous renal artery disease

- Renal vascular disease had the poorest survival estimates of all diagnoses for ESRD, with 25 months median length of survival and 5 and 10 year survival rates of 18% and 5% respectively. This survival was significantly less than for ADPCKD (the best survival rate).
- Diabetes mellitus was not compared head to head.

Prevalence of bilateral renal artery stenosis

Reference	Stenotic arteries	Bilateral	Method
	N	N(%)	
Holley 1964	159	105(66)	Autopsy
Wollenweber 1968	109	67(61)	Arteriogram
Dean 1981	41	14(34)	Arteriogram
Tollefson 1991	48	14(29)	Arteriogram
Harding 1992	192	52(27)	Arteriogram

From Rimmer JM, Gennari FJ. Atherosclerotic Renovascular Disease and Progressive renal failure. Ann Int Med, 1993;118:712-719

Natural history: The Prospective Trials

- Dean et al 1981 Arch Surg, 116:1408-1415
- Zierler et al 1996 Am J HTN, 9:1055-1061

Dean’s study

- 41 patients (23 M, 18 F) enrolled from 2580 hypertensive patients evaluated from 1971-1981 at *Vanderbilt U Med Cen*.
  - Recruitment details are referred back to a paper by *Foster et al in Ann Surg, 1973, 177:755-765* (the referring paper gave the pages as 765-775)

Dean’s study

- Foster’s study appears to be the one cited by most texts whereby renovascular hypertension is said to be the etiology of 5% of patients who have diastolic hypertension.
- It should be noted the author’s original sentence includes “in our opinion.” (i.e., unreferenced)

Dean’s study

- Foster’s study refers to 10 year study results, presumably starting in 1963, and 1070 patients originally studied (apparently this later grew to 2580 by 1981).
- Age 40-65
- They underwent an evaluation leading to renal arteriography.
- Those who had renal artery stenosis (RAS) the had split renal function studies and renal vein renins.

Dean’s study

- If either was positive, renovascular hypertension (RVH) was considered established
- 460 patients of the original cohort had RAS.
- Of those, 176 (39%) had RVH (or 16% of the original cohort).

Dean’s study

- After acceptance as an operative candidate, they were randomly assigned to drug therapy or operative treatment groups
- Baseline determinations were conducted and repeated at “predesignated intervals” or earlier if BP were not controlled (levels undefined).

Dean’s study

- 50 patients had been placed on the medical management protocol since 1971.
- 41 had atherosclerotic lesions and 9 had fibromuscular lesions.
- Of these 23 M and 18 F, the highest Bp’s ranged from 190/120 to 260/180. Means were not given. 18 were hyperlipidemic, only 3 were diabetic.

Dean’s study

- Follow-up ranged from 2-114 months.
- Details regarding patient dropout and intention to treat were not mentioned.
- Exclusion criteria not explicitly stated
- Only 6% of the final study participants were African American although 33% of the original cohort of 1070 were African American. The role of insurance was not addressed.

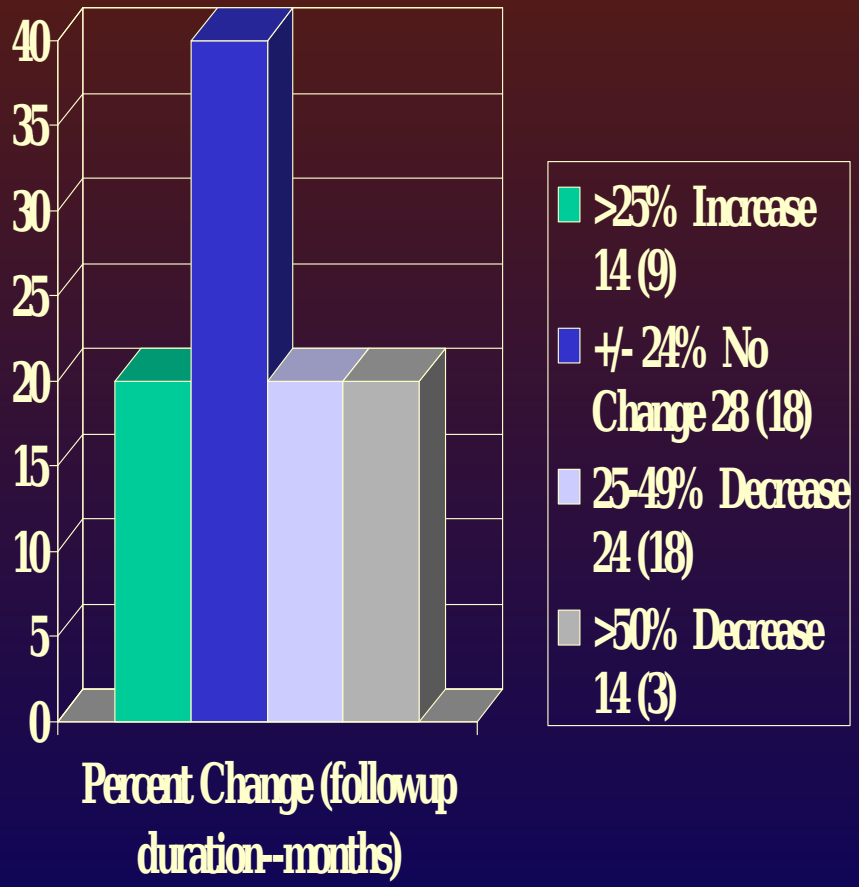
Baseline anatomic and renal function data

Aspect	*Range*	*Mean*
Serum creatinine, mg/dl	*0.6-2.6*	*1.3*
CrCl, ml/min	*15-140*	*71*
GFR, ml/min	*23-138*	*69*
Split renal function studies *Ipsilateral CrCl, ml/min* *Contralateral CrCl*	*2-79* *31-129*	*43* *66*
Renal length, cm *Ipsilateral kidney* *Contralateral kidney*	*7.8-17* *10.0-16.8*	*12.4* *13.7*

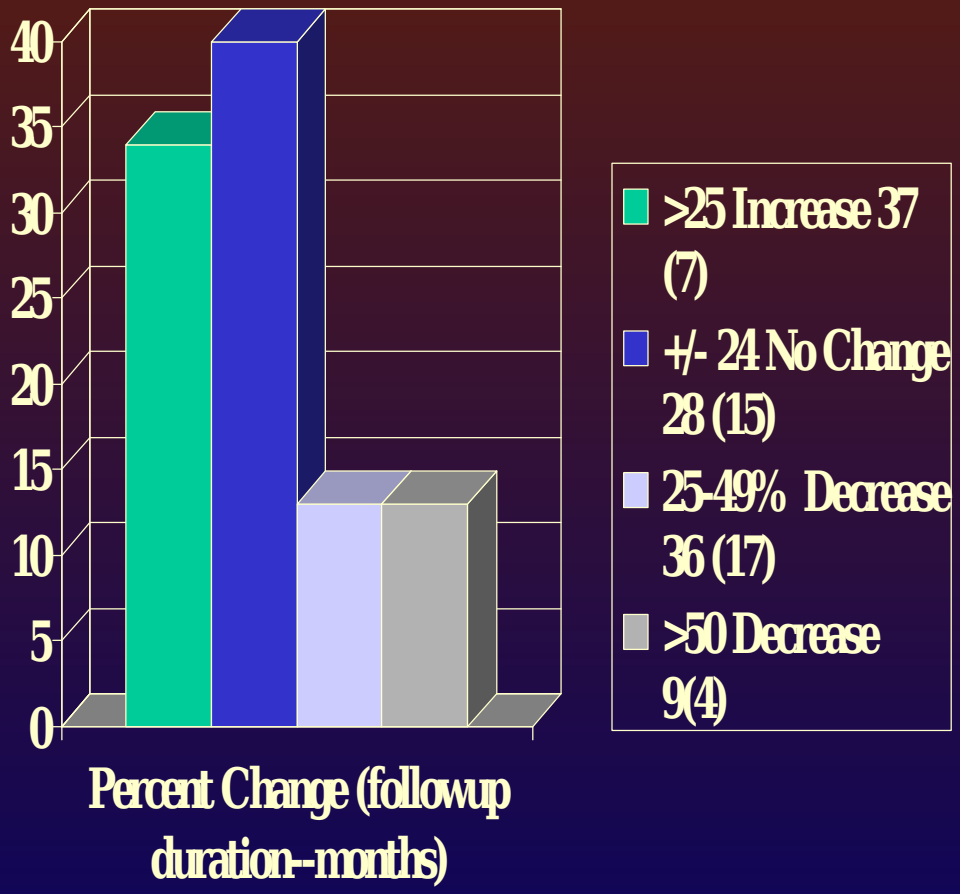
Progression of contralateral disease

Case	Initial Severity %	Final Severity %	Interval, mo
1	36	97	54
2	82	99	48
3	79	91	12
4	0	84	66
5	0	56	36
6	0	84	12

Ipsilateral side



Contralateral side



Percent change in individual kidney creatinine clearances as determined by split renal function studies during follow-up in

Frequency of severe deterioration in aspects of renal function

Aspect	*No. of Patients followed up*	*Mean Follow-up, Months*	*Failure Event*	*No. affected*	*% affected*
Renal length	*38*	*33*	*>10% decrease*	*14*	*37*
Serum creatinine	*41*	*25*	*>100% increase*	*2*	*5*
GFR or CrCl	*30*	*19*	*>50% decrease*	*1*	*3*

Summary

- From the previous table, failure events that warranted consideration of operative management occurred in 17 patients (41%), 15 (88%) of whom had “acceptable” control of BP by drug therapy alone (in follow-up varying from 19-33 months.
- BP targets NOT mentioned, but in Foster’s paper, cure was defined solely by diastolic blood pressure of <90 mm Hg. Systolic NOT mentioned.

Summary

- Only 2 of 10 patients without acceptable BP control had a severe decrease in renal length during follow-up.
- 12/14 patients having severe reduction in length did have acceptable BP control.
- Sample size and study design did not allow conclusions re role of BP.

Summary

- Calculation of a rate of progression was not felt possible, for patients seemed to have different degrees of vulnerability to progression.
- Some had rapid progression and others had very stable courses.
- Factors predicting progression were not identified (lipids, BP). Again, targets not mentioned.
- It was not mentioned if any patients died or reached ESRD requiring dialysis during the study period.

Conclusions

- The authors attempted to conclude that adequate blood pressure control might not be helpful and might even be detrimental in progression of renal arterial disease, although they admit the study did not directly support this conclusion.
- This conclusion has been extrapolated to mean that **higher than normal BP's are recommended for patients with renal arterial disease.**
- It must be emphasized this study **does NOT support that conclusion.**

Zierler's study

- *AJH, 1996.*
  - 36 M, 40 F recruited from University of Washington, Seattle.
- Average age 66
  - Ethnic breakdown not mentioned.
  - Entry consideration were hypertension, decreased renal function, or both.

Zierler’s study

- Patients with at least one abnormal renal artery by duplex ultrasound scanning and who were NOT considered candidates for immediate surgical or radiologic intervention were eligible for recruitment (the numbers of patients thus excluded was not mentioned).

Zierler's study

- 122 patients had been recruited.
- 46 were excluded
  - 27 had no follow-up studies
    - 8 presumed fibromuscular dysplasia
    - 8 had bilateral renal artery interventions
    - 2 withdrew
    - 1 had inadequate duplex study

Zierler’s study

- After baseline evaluation, patients with at least one high grade renal artery stenosis (>60% diameter reduction) were followed at 6 month intervals
- Those with less severe lesions followed at 12 month intervals

Zierler’s study

- In addition to complete renal artery duplex scan, baseline and follow-up visits included risk factors for atherosclerosis (AS) (smoking, diabetes, hypercholesterolemia), extra-coronary AS, and any interventions for treatment of arterial disease.
- Duration and treatment of HTN were recorded

Zierler’s study

- BP’s recorded in both arms.
- BUN and creatinine also recorded.
- 7 patients with high grade renal artery lesions had therapeutic interventions during follow-up, including six balloon angioplasties and one nephrectomy.
- Analysis of their disease included only the period up to their intervention.

Cumulative incidence of renal artery disease progression according to severity of disease at baseline

Follow-up interval in months

Baseline Renal Duplex	0	12	24	36
Normal				
Progression	0 (-)	0 (-)	0 (-)	8 (0-19)
(0.95 CI)	36	33	27	22
N				
<60% Stenosis				
Progression	0 (-)	30 (15-45)	44 (25-63)	48 (28-68)
(0.95 CI)	35	22	14	11
N				
>60% Stenosis				
Progression	0 (-)	4 (0-9)	4 (0-9)	7 (0-16)
(0.95 CI)	61	43	31	20
N				
All Progressions				
Progression	0 (-)	10 (5-15)	14 (7-21)	20 (12-28)
(0.95 CI)	132	98	72	53
N				

Association of Categorical risk factors with renal artery disease progression

Baseline risk factor	*N Showing disease progression*	*Percent*	*P*
Gender	Male (36)	31	.05
	Female (40)	52	
Blood Pressure control	>140/90 (66)	47	.13
	<140/90 (8)	13	
Current/former smoker	No (19)	42	NS
	Yes (68)	42	
Diabetes mellitus	No (68)	40	.27
	Yes (8)	62	
H/o MI	No (50)	40	.61
	Yes (26)	46	
Claudication	No (69)	42	NS
	Yes (7)	43	
CEA	No (68)	38	.06
	Yes (8)	75	
High Cholesterol	No (45)	42	.90
	Yes (27)	41	

Association of continuous risk factors with presence or absence of disease progression

Baseline Risk Factor	Disease Progression: No (Mean +/- SD)	Disease Progression: Yes (Mean +/- SD)	P
Age	66 (9-44)	69 (8-32)	.08
Systolic Blood Pressure	164 (22-43)	171 (20-32)	.15
Diastolic Blood Pressure	85 (7-43)	85 (10-32)	.87
Blood Urea Nitrogen	21 (10-32)	26 (22-26)	.26
Creatinine	1.3 (0.6-32)	1.6 (1.6-26)	.39
Pack years of smoking	27 (30-39)	39 (37-28)	.14
	(SD-N)	(SD-N)	

Summary

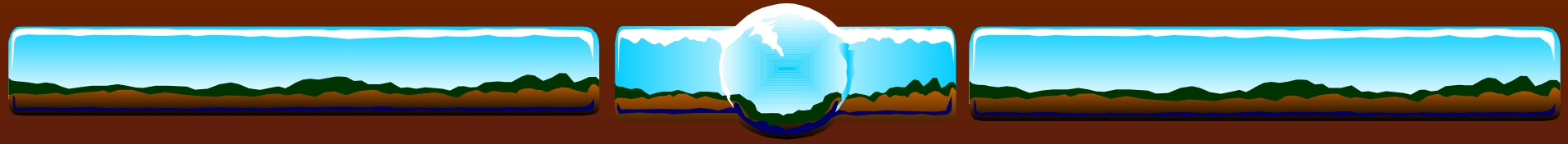
- Renal artery disease progression occurred at an average of 7% per year for all categories of baseline disease combined.
- Progression differed markedly depending on the baseline disease status.
- Normal vessels progressed very slowly over 36 months (2.7% per year) .

Summary

- Patients with <60% stenosis had most rapid rates of progression (48% to >60% stenosis at 36 months, 16% per year), although serial creatinines were not mentioned in the study and serial GFR's were not performed.
- Progression for patients with >60% stenosis was defined as total occlusion, and this occurred in only 7% at 36 months (2.3% per year). This group included the most patients of any single group in the study.

Summary

- It was not mentioned if any patients died or reached ESRD requiring dialysis during the study period.



Conclusions

- This study confirms that diastolic BP of 85 had no impact on disease progression.
- The study implies that a difference of systolic blood pressure from only 171 to 164 had a trend to significantly less disease progression (p=.15).
- Sample size of 142 patients in each group would have reached statistical significance, even at this relatively high systolic pressure.

Conclusions

- It should also be noted that only 11% of the study participants were maintained at a BP <140/90.
- Of this group, only 13% progressed vs. 47% with higher BP (p=.13)
- Sample size could not be calculated since means and SD not given.

Conclusions

- The study doesn’t mention whether the patients with lower BP were also the ones with better disease at baseline.
- Type of BP medications used also were not mentioned.
- “Adequate” BP control has NOT been given a fair shot in medical therapy of atheromatous renal artery disease.

Conclusions

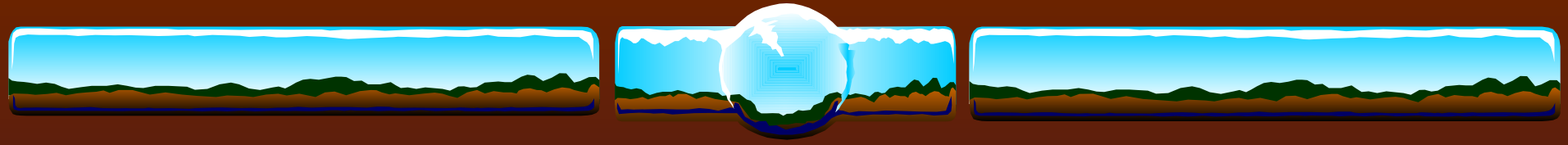
- The potential usefulness of other medical treatments, such as lipid medications, folic acid, antioxidants, etc., remain unknown.

Zierler's Study

- Additional patients and longer term follow-up on the patients in the prior study were presented by Caps MT et al in Circulation, 1998, 98(25), Dec 22/29, PP 2866-2872.
- In this study, a systolic BP ≥160 mm Hg resulted in a relative risk of 2.1 ($p<0.006$)

Zierler’s study

- The industrious Zierler’s group also presented information from these patients about the risk of renal atrophy in Caps MT et al, Kidney Int, 1998, 53, 735-742.



Zierler and Cap's KI study

N of Kidneys demonstrating atrophy	N subjects[a]	Mean Δ [Creat]/year Mg/dl/yr	P value[b]
0	86	+0.01	--
1	19	+.08	0.4
2[c]	7	+.033	0.03

a 112 of 122 patients had >2 creatinine determinations during the study permitting linear progression to be performed.

B P=0.03 for the test for a trend between creatinine concentration change and number of shrinking kidneys; listed P values are for t-tests with "0 shrinking kidneys" as the referent category.

C One subject in this group had one kidney that shrank during the study contralateral to an atrophic kidney at baseline.

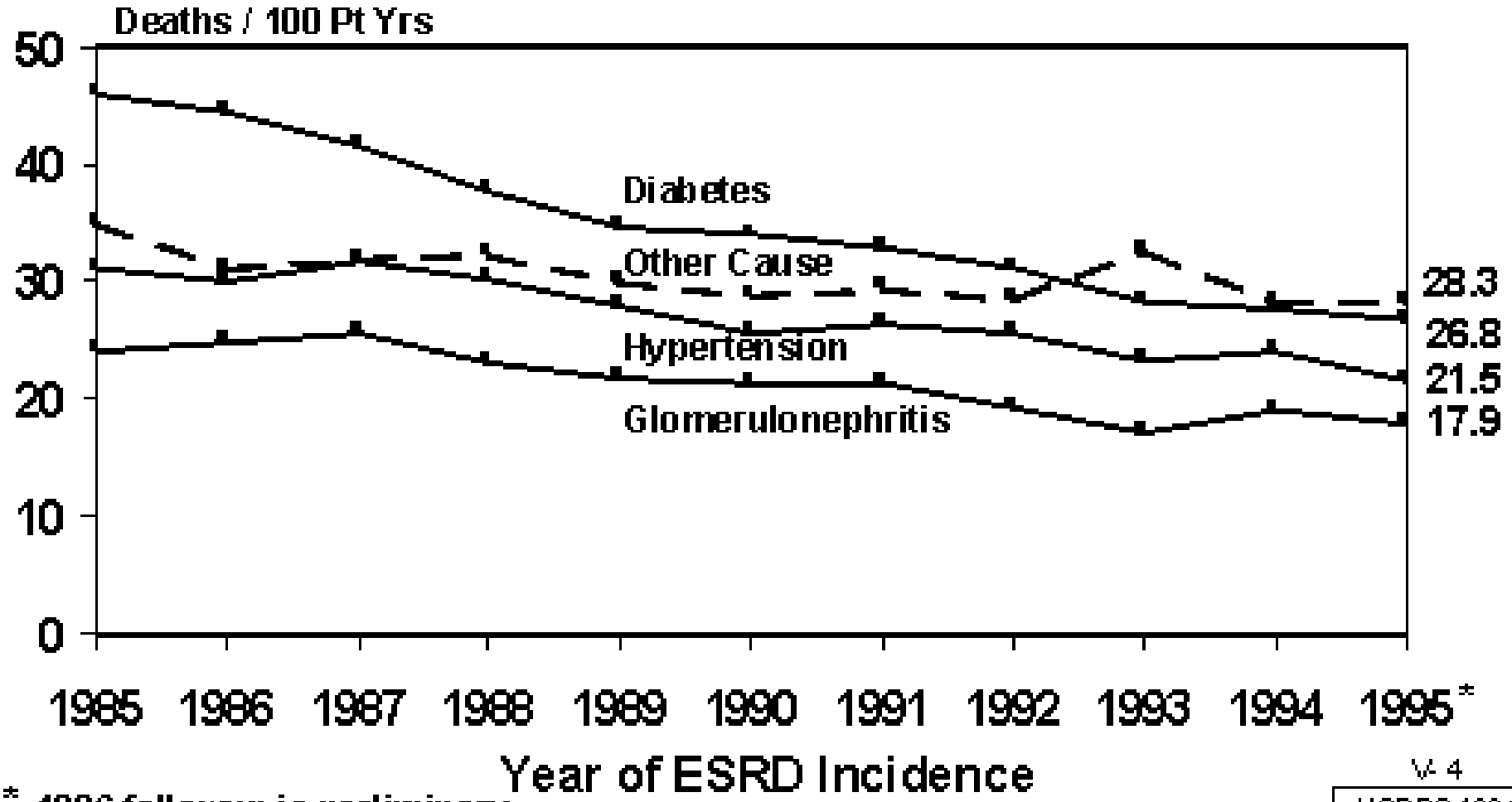
Survival in Renal Vascular Disease

- Another retrospective study followed 896 patients selected from 1305 patients undergoing cardiac catheterization for other reasons over a 5 month period at Duke by *Conlon et al* (1).
- Details of baseline demographics and pre-procedure renal function were not specified, however none were on dialysis at the start of the study.

Survival in Renal Vascular Disease

- Four year unadjusted survival was 67% for those with >50% RAS, vs. 88% for patients without significant RAS (p<.0001).
- Adjusted survival was 88% for those with RAS vs. 96% for those without (p<.0002).
- The major cause of death for those with or without RAS was cardiovascular disease.
- Among patients who died, it was rare for patients to have progressed to ESRD.

Adjusted 1-Year Death Rates for Dialysis Patients By Primary Cause of ESRD and Year of Incidence, 1985-95



* 1996 followup is preliminary

Expected Remaining Lifetimes for U.S. Population (1990), All ESRD Patients[1] (1996) and Dialysis Patients (1996) by Age, Race and Sex

	U.S. Population, 1990[2]				ESRD population, 1996[4]				Dialysis population[3,4], 1996			
	Black		White		Black		White		Black		White	
Age	M	F	M	F	M	F	M	F	M	F	M	F
0-14	61.5	67.0	71.1	78.0	29.0	27.6	33.1	32.1	20.3	19.7	18.8	18.8
15-19	51.3	57.4	58.5	65.0	22.7	21.5	24.5	23.5	19.3	18.4	16.4	15.2
20-24	46.8	52.9	53.8	60.1	19.5	18.5	21.3	20.3	16.8	15.9	14.0	13.0
25-29	42.5	48.7	49.2	55.3	16.8	16.5	17.8	17.5	14.5	14.1	11.3	11.0
30-34	38.2	44.6	44.6	50.4	14.6	14.5	15.0	14.9	12.7	12.5	9.4	9.3
35-39	34.1	40.6	40.0	45.6	12.8	12.8	12.6	12.6	11.3	11.4	8.0	7.9
40-44	30.1	36.8	35.4	40.8	11.1	10.9	10.5	10.6	10.0	9.8	6.9	7.1
45-49	26.2	32.4	30.9	36.1	9.4	9.3	8.7	8.7	8.6	8.5	6.1	6.3
50-54	22.5	28.2	26.5	31.5	7.9	7.7	7.1	6.9	7.3	7.1	5.2	5.2
55-59	19.1	24.3	22.4	27.0	6.7	6.6	5.6	5.6	6.3	6.3	4.4	4.5
60-64	16.0	20.6	18.6	22.8	5.5	5.5	4.4	4.5	5.2	5.3	3.7	3.9
65-69	13.3	17.2	15.2	18.9	4.4	4.5	3.5	3.6	4.2	4.4	3.1	3.3
70-74	10.8	14.2	12.0	15.2	3.6	3.7	2.9	3.0	3.5	3.7	2.7	2.9
75-79	8.8	11.3	9.3	11.8	2.9	3.0	2.4	2.5	2.9	3.0	2.4	2.5
80-84	6.9	8.7	7.0	8.8	2.5	2.5	2.1	2.1	2.5	2.5	2.1	2.1
85+	5.4	6.5	5.1	6.1	2.1	2.0	1.7	1.7	2.1	2.0	1.7	1.7

[1] Includes patients treated with either dialysis or transplantation.

[2] Vital Statistics of the US, Vol 2,1990: Mortality, Part A, Table I-9.

[3] Mortality followup is censored at transplant.

[4] Death rates used for these calculations exclude dialysis unrelated deaths.

Source: Reference Table D.2 and Special Analysis

USRDS 1998

Survival in Renal Vascular Disease

- RAS contributed to, but was only a secondary cause of, death in these patients.
- Although renovascular disease frequently progresses, death from coronary or cerbral vascular disease often occurs before a decline in renal function.
- What would be useful would be a five year survival estimate from non-renal disease to determine if the patient would benefit from intervention.

Incidence of ESRD in medically treated patients with severe bilateral RAS

- Retrospective 5 year study of 51 patients with chronic renal failure (mean GFR 39 cc/min, range 15-80) in England by *Baboolal et al* (1).
- All patients who underwent renal angiography from 1986-1993 were followed for 5 years.
- Bilateral RAS defined as >90% stenosis in one kidney and >50% stenosis in the contralateral kidney.

Incidence of ESRD in medically treated patients with severe bilateral RAS

- Interventions were not performed because:
  - patient preference
  - lesions not amenable
  - kidneys were too small to salvage
  - patients not amenable
  - One patient was excluded for parenchymal renal disease and 15 excluded for incomplete medical records.
  - Diabetic patients were excluded.

Incidence of ESRD in medically treated patients with severe bilateral RAS

- MAP at time of angiography was 118, and at latest follow-up was 110 (MAP 106 for typical target 140/90).
- The number of medications required to control blood pressure but maintain GFR increased over the time of the study from an average of 2 to 4.
- 38% of patients died within two years of angiography.

Incidence of ESRD in medically treated patients with severe bilateral RAS

- Crude mortality at 5 years was 45%.
- Death in all cases was due to cardiovascular disease.
- The crude incidence of ESRD was 12%.
- If the data are censored for patient mortality, the percent reaching ESRD was 30% at five years.

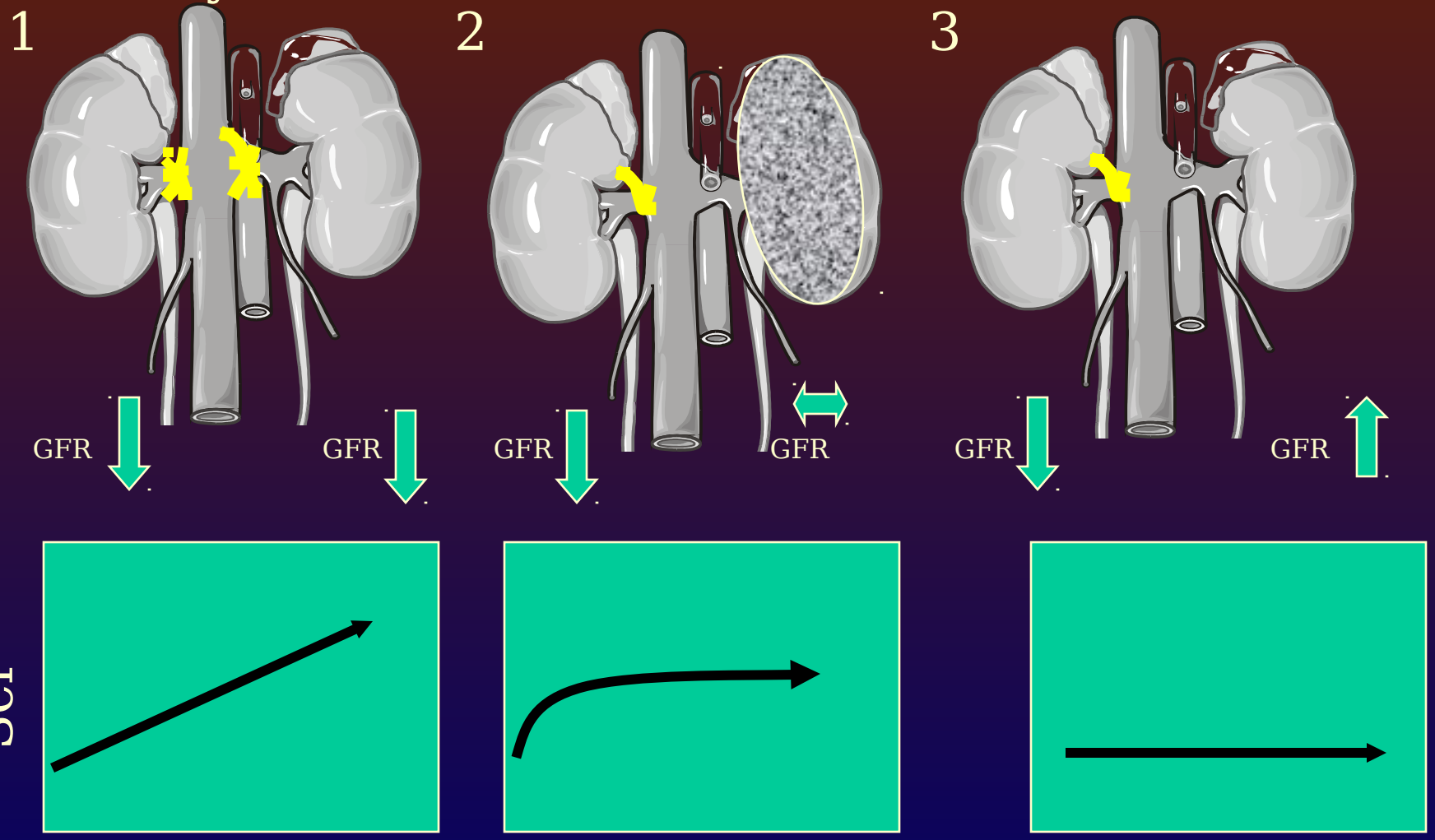
Demographics of fatalities vs survivors

	ESRF	Died	Survivors
N	6	23	22
Age(yr)	62	59	63
Sex (male:female)	2:4	13:10	13:9
Mean arterial pressure (mm Hg)	115	117	121
Kidney size (occluded) (cm)	7.0	7.4	7.4
Kidney size (stenosis)	8.5	10.7	9.8
GFR at angiography (cc/min)	25 (15-56)*	45 (17-71)	41 (21-80)
Rate of change of GFR (cc/min/yr)	8 (3-13)	3.5 (1-15)	3.1 (1-11)
Ischemic heart disease (%)	67	85	74
Peripheral vascular disease	66	52	64
Cerebral vascular disease	33	48	41
Smoker	83	64	86

Incidence of ESRD in medically treated patients with severe bilateral RAS

- Six patients received ACE before angiography, which was not associated ith a reduction in GFR, not did removal of ACE improve GFR.
- However, a prospective trial in the Netherlands demonstrated that even in severe bilateral RAS, decrement in GFR or rise in creatinine often does not occur with the use of ACE until a diuretic is added (1) (more about use of ACE in the screening section).

Potential effect of ACE inhibitors on GFR and Scr in patients with hemodynamically significant renal artery stenosis



(Adapted From Rimmer et

Reports of Serial Angiograms

Reference	Months of Follow-up	Patients	Progression	Total Occlusion
	n-n	N	N(%)	N(%)
Wollenweber 1968	12-88	30	21(70)	NA
Meaney 1968	6-120	39	14(36)	3(8)
Dean 1981	6-102	35	10(29)	4(11)
Schreiber 1984	12->60	85	37(44)	14(16)
Tollefson 1991	15-180	48	34(71)	7(15)
Total		237	116(49)	28(14)

NA= not available. Progression of disease includes worsening of already stenosed renal artery or development of contralateral stenosis.

From Rimmer JM, Gennari FJ. Atherosclerotic Renovascular Disease and Progressive renal failure. Ann Int Med, 1993;118:712-719

Overall Conclusions

- Rate of anatomic progression and progression to ESRD is fastest in those with more severe disease at baseline (>60% stenosis anatomically and GFR <25 cc/min).
- Mortality in these patients is such that they **usually do not survive to reach ESRD.**

Overall conclusions

- What is needed is a more sophisticated tool to determine beforehand which patients would survive to reach ESRD and therefore benefit from intervention.
- More work needs to be done to see what, if anything, can reduce the cardiovascular mortality of these patients regardless of whether they reach ESRD.

Controversies

- If we agree on the approach to patients with severe bilateral RAS who are reasonable candidates for intervention, what about patients with severe **unilateral** RAS? In the absence of intractable hypertension, does intervention on the diseased kidney improve risk of progression to ESRD, or mortality?

Controversies

- Is “adequate” blood pressure control helpful or harmful in patients with bilateral RAS? In patients with unilateral RAS?
- What targets other than blood pressure are helpful in medical management?